# Latex Hypersensitivity

## Colonel Larry Hagan

# Background

# Latex Hypersensitivity-A New Phenomenon?

- First case reported in Germany in 1927
- Next published case reported 52 years later*
- Earliest North American reports in 1989
- Many cases since, including deaths (~15)
- Universal precautions (AIDS epidemic) → increased use of latex gloves
- Increased demand → change in manufacturing techniques → increased antigen

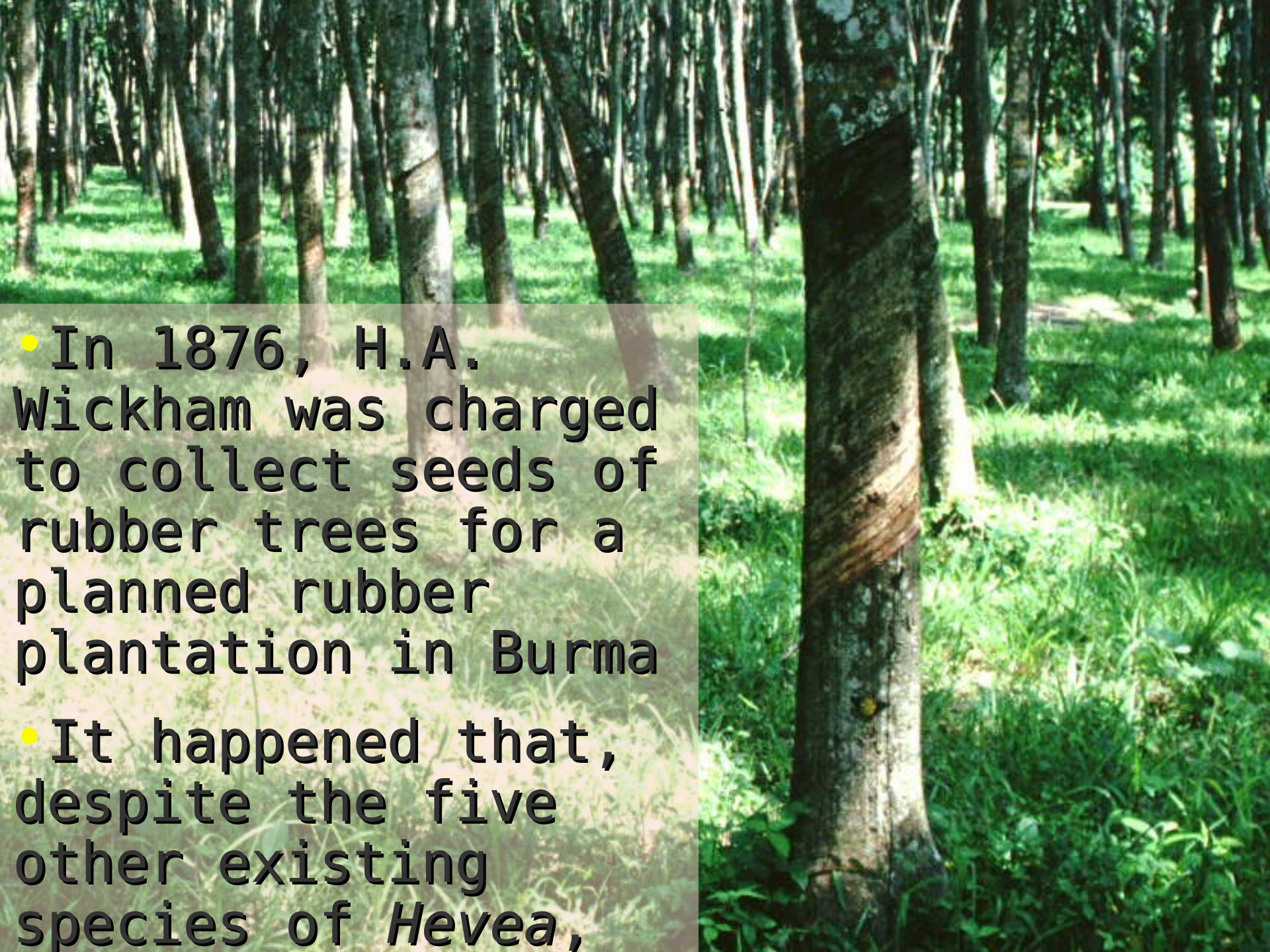
* Br. J. Dermatol. 1979

# Definition of Latex

- Natural rubber
- **NOT** water soluble acrylic-based paints

# Origin of Latex

- **Natural rubber is derived from the milky sap of the *Hevea brasiliensis* tree**
  - **Originated in Central and South America**
  - **Now cultivated in South Asia (primarily Malaysia) and Africa**



- In 1876, H.A. Wickham was charged to collect seeds of rubber trees for a planned rubber plantation in Burma
- It happened that, despite the five other existing species of *Hevea*,

- The Indian government was to fund the plantation but, due to cuts, found it was impossible
- The seedlings were then sent to the Singapore

# Origin of Latex

- A spiral groove is cut in the tree and a cup at the base of the spiral collects the latex
- **Ammonia** placed in the cup prevents coagulation and bacterial contamination
  - Product is **ammoniated latex** concentrate: used for **dipped products**, adhesives, foam, balloons, condoms

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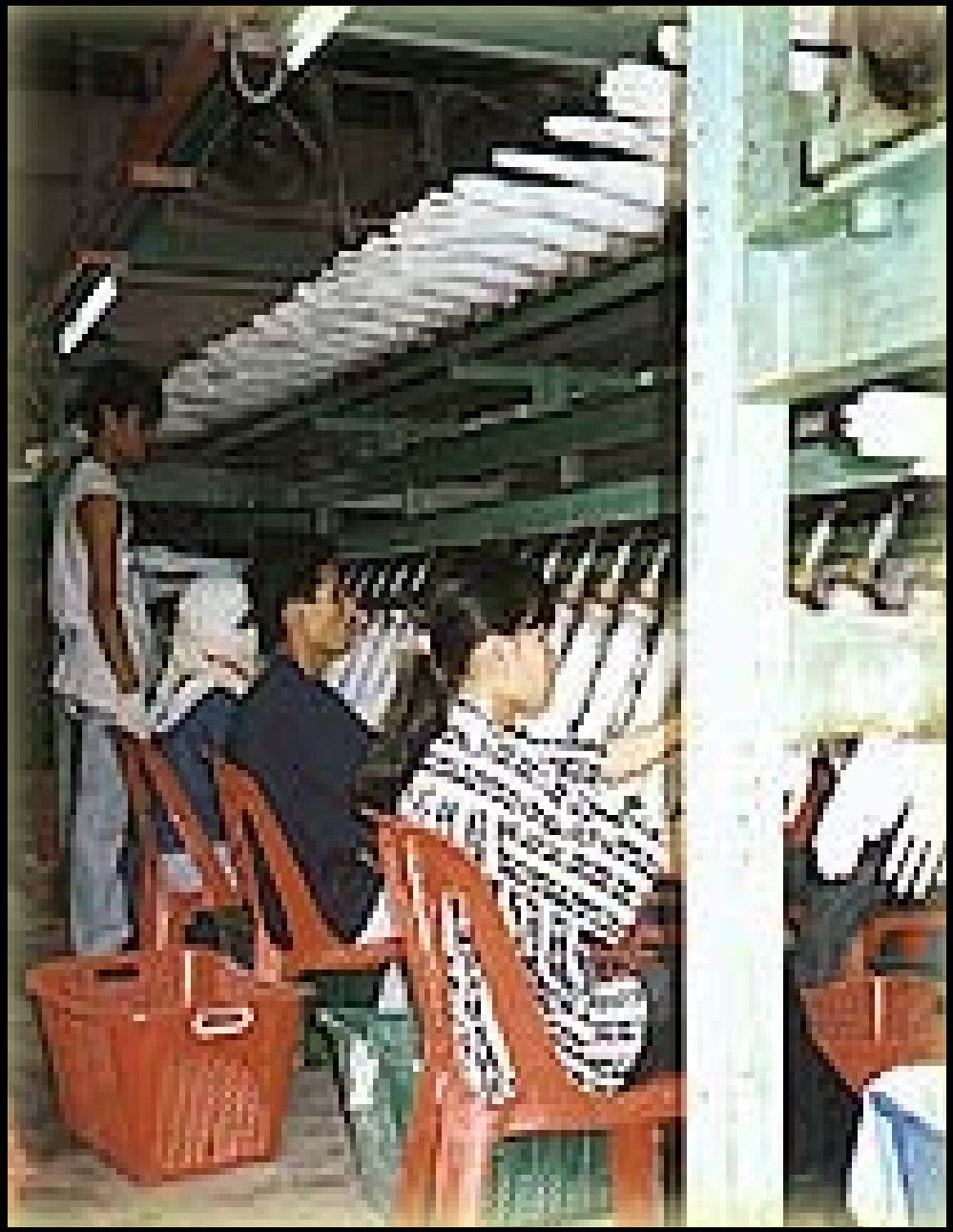
# Processing Latex

- Collected latex is treated with a number of chemicals
  - calcium alginate
  - $Na^+$ pentachlorophenate
  - tetramethylthiuram disulfide
  - $Na^+$ dimethyldithiocarbamate
  - zinc oxide
- Vulcanized by slow heating with sulfur
  - Improves elasticity and thermostability
- Improves commercial properties of latex

CLT
NO ENTRY

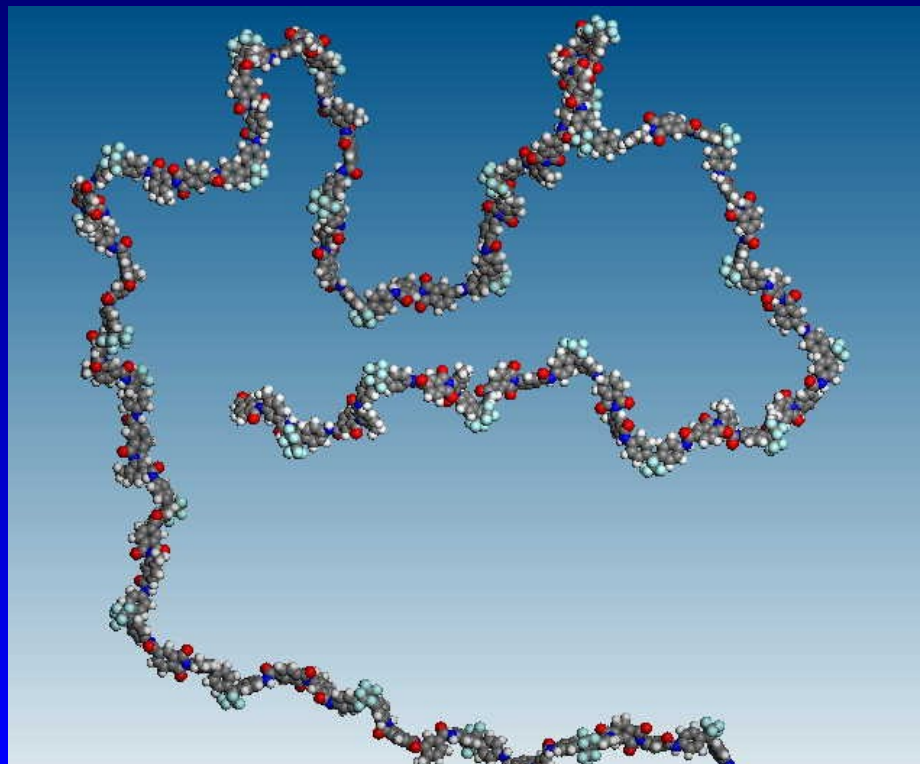
# Making of Latex Gloves

- Porcelain molds are covered with coagulating salts, dipped into the vulcanized latex, allowed to dry, and washed
- The gloves are pulled off the mold and powdered



# Chemistry of Latex

- **Polymerized Isoprene subunit (five-carbon isopentenyl diphosphate) with lengths that run in the thousands**
- **Rubber elongation factor and other enzymes**



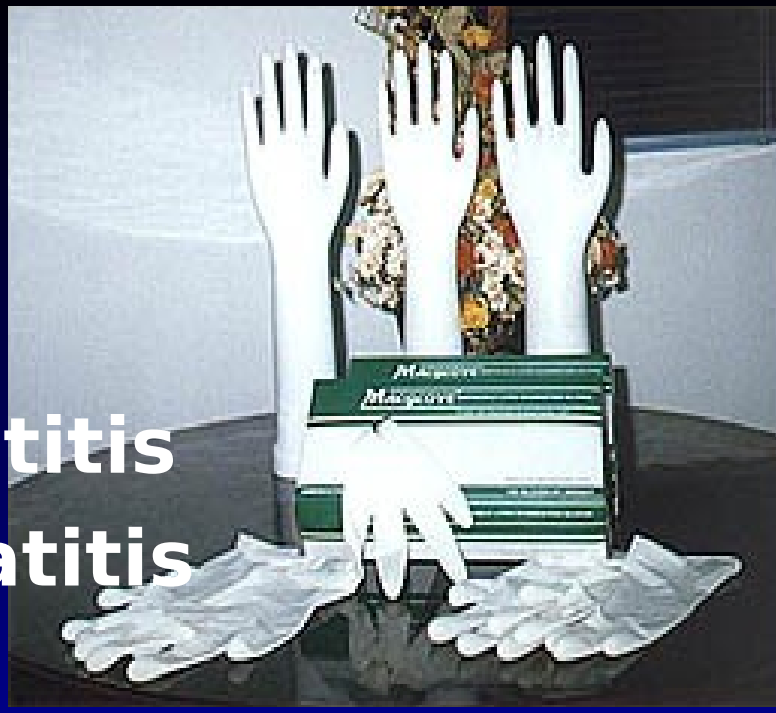
# Chemistry of Latex

- Basic **functional unit** is the **rubber particle**
  - Spherical droplet of **polyisoprene**
  - Coated with a layer of **protein**, **lipid** and **phospholipid** to provide structural integrity

# Glove Powder

- Talc rarely used (granuloma formation)
- Cornstarch most common
  - Cornstarch: contains no protein
- Allergens can be adsorbed to the powder
  - Higher concentration of latex antigen on inside of glove
  - Can become airborne
  - Inhalation → immediate hypersensitivity
- Major factor in latex hypersensitivity?

# Types of Reactions



- Irritant contact dermatitis
- Allergic contact dermatitis
- Contact urticaria
- Bronchospasm from inhalation of powder
- Angioedema
- Life-threatening anaphylaxis

# Irritant Contact Dermatitis

- Occurs especially in atopic patients
- May be mechanically provoked by glove powder crystals → break in the stratum corneum barrier of the skin
- Associated with occlusion and the use of disinfectants, mainly in the O.R.

# Allergic Contact Dermatitis (Type 4)

- Described in 1935
- **Accelerators:** Thiurams, carbamates, mercaptans
- **Anti-oxidants:** p-phenylenediamine, phenols, quinolines
- **Vulcanizers:** Dithiodimorpholine, benzoyl peroxide
- Organic **pigments**
- Glove powder ingredients?

# Allergic Contact Dermatitis

- Rubber glove eczema in **health care workers**
- Condom dermatitis
- Rubber factory workers
- Stomatitis to rubber orthodontic appliances
- Diagnosis: **patch testing**

# Irritant vs. Allergic Contact

- Irritant dermatitis develops quickly and resolves quickly
  - Sharply demarcated
- Allergic contact dermatitis takes several days to develop, and resolves slowly
  - More diffuse inflammation

# Type I Reactions - IgE Mediated

- First described in modern times in 1979*
- Since then more than 1,100 serious reactions to latex have been reported to the FDA
  - 15 of these caused death and were associated with the use of latex-cuffed barium enema kits

* Contact urticaria to rubber Br J Derm 1979;101:597-8

# Type I Reactions - IgE Mediated

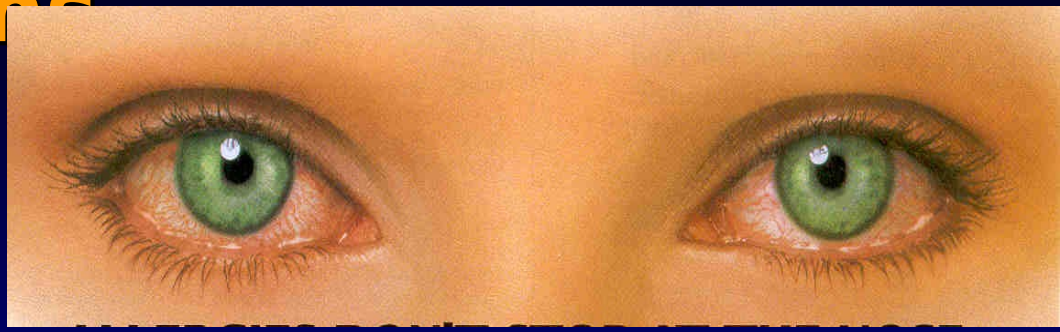
- A progression of latex-associated symptoms may occur*

  Dermatitis → urticaria → systemic symptoms

* Charous BL: Occupational latex exposure: characteristics of contact and systemic reactions in 47 workers. JACI 1994,94:12-180

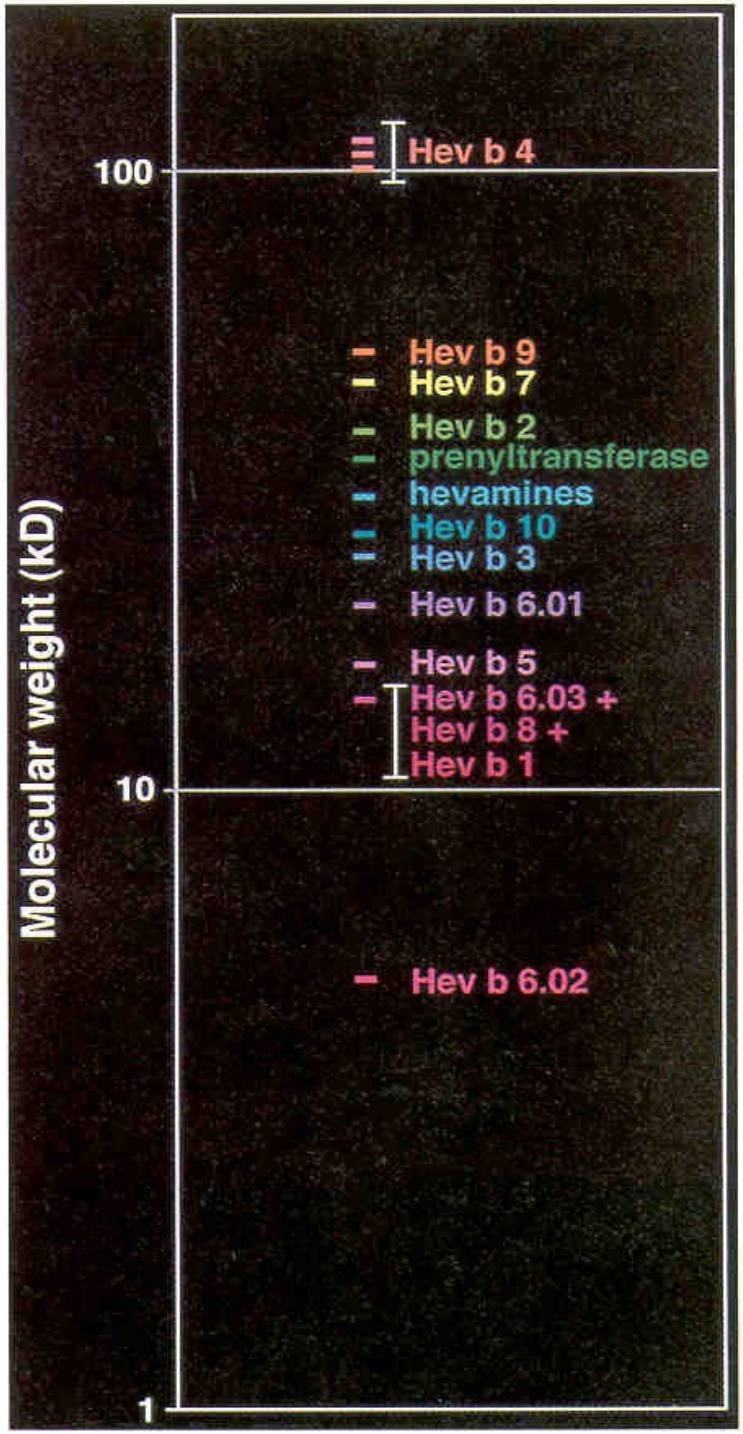
# Type I Reactions

- Local or systemic urticaria, rhinitis, conjunctivitis, bronchospasm, and anaphylaxis
- **IgE-mediated**: skin testing, RAST
- Elicited by the **peptides** present in natural rubber



# Type I Reactions- Latex Allergens

- Proteins with Mol Wt 2-30 kd
- Allergens vary with different lots and production methods
  - Range of latex antigen can vary **400-fold** between different brands of gloves
- One glove antigen has been identified that is not present in the sap
  - ? **Neoantigen** produced by processing




# Latex Allergens*

- **Hev b 1-15**
- **Hev b 1 & Hev b 3 are major allergens for children with congenital anomalies**
  - **Less soluble than other antigens**
- **Hev b 2 & Hev b 4: Health Care workers**
- **Hev b 5 recognized by both Health Care workers and children**

*JACI 2000;105:1054-

# Who's At Risk?

# Prevalence in General Population

- Ylitalo: 3269 children, 1% latex allergic[1]
- Porri: 365 routine check-ups, 2.3% latex SPT positive [2]
- Merrett:  1426 blood donors, 7.4% latex antibody positive[3]
- Ownby: 1000 blood donors, 6.5% latex antibody positive[4]
- Novembere: 326 children, 3% PST positive, 1.5% clinical allergy[5]


1. JACI. 1997;100:606-612
2.  JACI. 1995;95:154
3. JACI. 1995;95:154
4. JACI. 1994;93:282

## Incidence of Sensitization, symptoms, and Probable Occupational Rhinoconjunctivitis and Asthma in Apprentices Starting Exposure To Latex*

- 110 subjects starting a dental hygiene program
- Followed for 20-32 months
- 7 (6.4%) developed skin test sensitivity
- 6 of 7 (5%) developed cutaneous symptoms
- 2 (1.8%) developed rhinoconjunctivitis
- 1 (0.9%) developed respiratory symptoms
- 5 (4.5%) developed changes in methacholine responsiveness

*JACI 2001,107:921-3

# Risk Groups

- **Health care workers**
- **Spina bifida**
- **Urogenital abnormalities**

*All characterized by high degree of exposure to rubber*

- **? Cross reaction with avocado, banana, chestnut, celery, fig, papaya, passion fruit, peach, tomato, kiwi**
- **Atopic individuals**
- **HLA DR4 & HLA DQ8**

# Spina Bifida Patients*

- **65%** of 76 patients **skin test positive** to latex
- **49%** of latex-positive group had histories of **immediate reactions** to latex
- Latex-positive group had a higher mean number of **surgical procedures** (**12.67** vs. 6.89)
- Higher incidence of **atopy** in the latex-positive group (**41%** vs. 19%)

*Cross J et al. Evaluation of latex allergy in patients with meningomyelocele. Annals of Allergy. 1992;69:207-11.

# Health Care Workers--Nurses*

- 197 OR nurses with history of latex exposure were skin-tested
- 10.7% positive
- 4.4 times more often in atopic nurses

*Lagier F et al. Prevalence of latex allergy in operating room nurses. JACI. 1992;90:319-22.

# Latex-Fruit Syndrome

- **Class I chitinases** are main cross-reacting allergen*
  - Panallergens, widely distributed in plant kingdom, especially in foods
  - Anti-insect properties
  - Heat labile
- Unclear whether patients allergic to these fruits constitute an independent risk group
  - Additional cross-reactivities reported between latex, **ragweed** and **blue grass**
- Implications for clinical use not known

*JACI

# Type I Reactions--Operating Room

- A great amount of exposure to latex occurs in the OR
- Latex antigen exposure by various routes: **cutaneous, percutaneous, mucosal, parenteral, inhalational**
- Direct mucosal and parenteral routes pose the greatest risk for anaphylaxis

# Threshold Latex Aeroallergen Reaction Levels*

- Latex sensitization level: 0.6 ng/m$^3$
- Hospital Room where latex gloves are being used: 60 to 600 ng/m$^3$

*JACI 2000;105:1054-62

# Threshold Latex Aeroallergen Sensitization Levels*

- Unknown if sensitization occurs via aeroallergen route alone or mainly by contact
  - 18 ng/40 hr week inhaled
  - Gloves contain 600 μg of latex allergen per gram of glove

*JACI 2000;105:1054-62

# Diagnosis

# Diagnosis

## Identify high-risk patients

- Health care workers
- Spina bifida or urogenital abnormalities
- History of rubber-induced reactions
- Allergic reactions of unknown etiology
  - Anaphylaxis during surgery

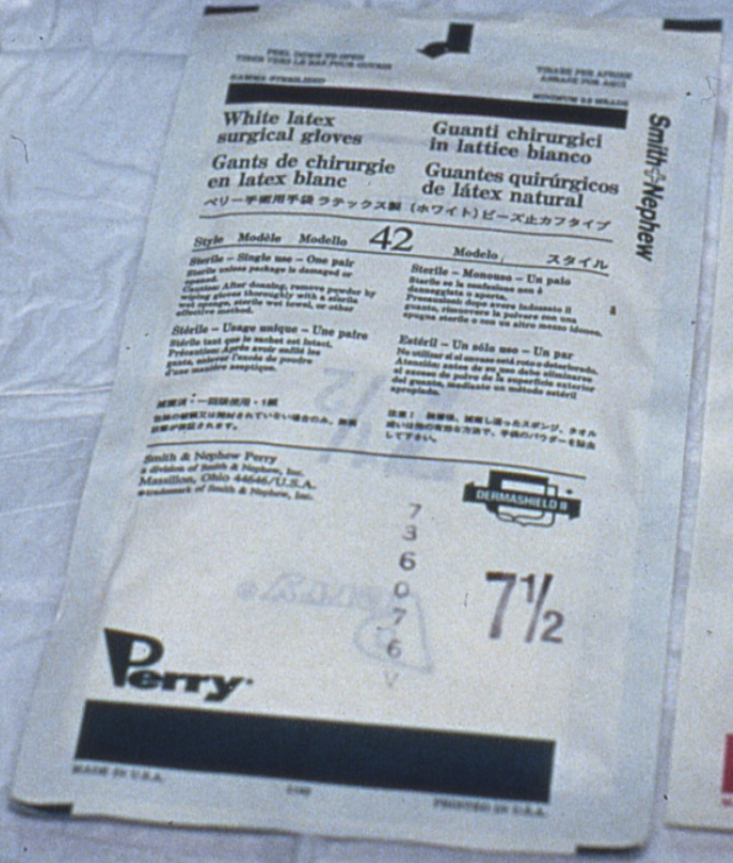
# Diagnosis--Skin Testing

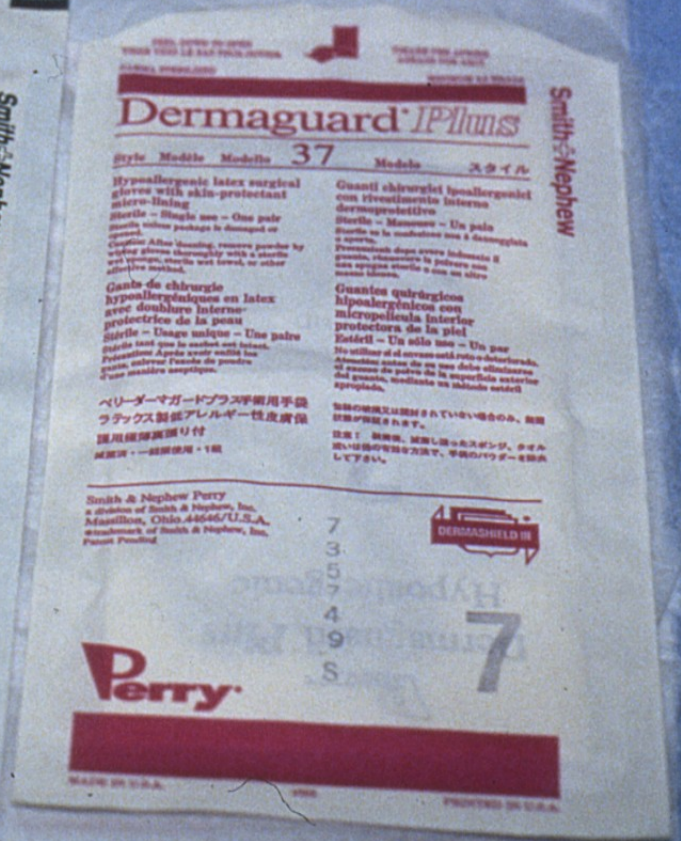
- Commercial extracts unavailable, but easily made
- Latex reagent currently under investigation
- Use the same lot of gloves that caused the reaction
- In one study, prick skin test was 100% sensitive and 99% specific*
- Higher incidence of systemic reactions than with other extracts?: nonstandardized extracts

*Moneret-Vautrin: JACI 1993; 92;668-77

# Glove Extraction Technique

100 DISPOSABLE
LATEX EXAMINATION GLOVES
PRODUCT OF MALAYSIA


White latex surgical gloves
Guanti chirurgici in lattice bianco
Gants de chirurgie en latex blanc
Guantes quirúrgicos de látex natural
ペリー手術用手袋 ラテックス製（ホワイト）ビーズ止カフタイプ
Style Modèle Modello 42 Modelo スタイル
Sterile – Single use – One pair
Stérile – Usage unique – Une paire
Sterile – Monouso – Un paio
Estéril – Un sólo uso – Un par
Smith & Nephew Perry
a division of Smith & Nephew, Inc.
Massillon, Ohio 44646/U.S.A.
DERMASHIELD III
7 3 6 0 7 6
7 1/2
Perry
MADE IN U.S.A.
PRINTED IN U.S.A.
Smith & Nephew


Dermaguard Plus
Style Modèle Modello 37 Modelo スタイル
Hypoallergenic latex surgical gloves with skin-protectant micro-lining
Guanti chirurgici ipoallergenici con rivestimento interno dermoprotettivo
Guantes quirúrgicos hipoalergénicos con micropelícula interior protectora de la piel
ペリーダーマガードプラス手術用手袋
ラテックス製低アレルギー性皮膚保護用超薄裏張り付
Smith & Nephew Perry
a division of Smith & Nephew, Inc.
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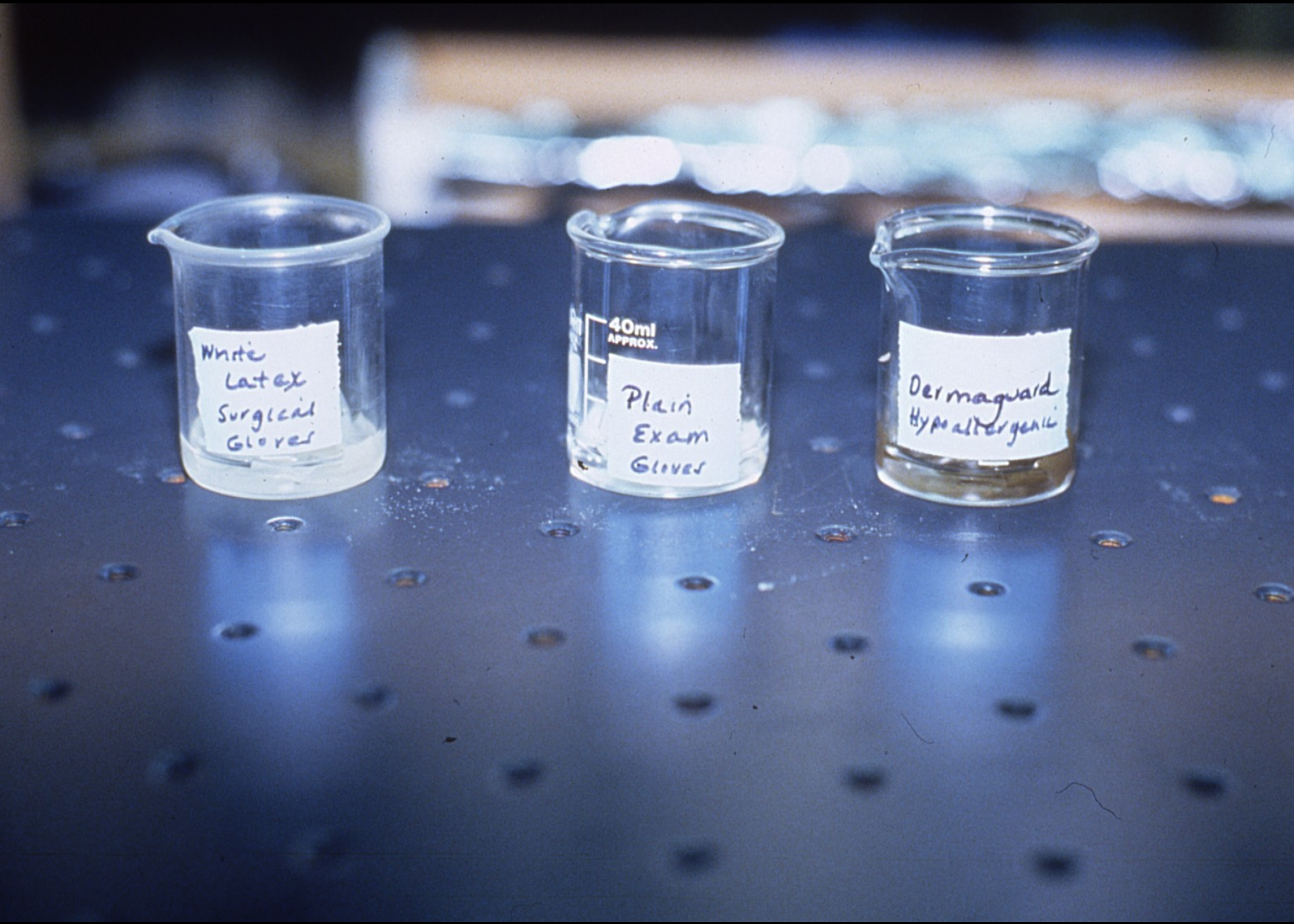
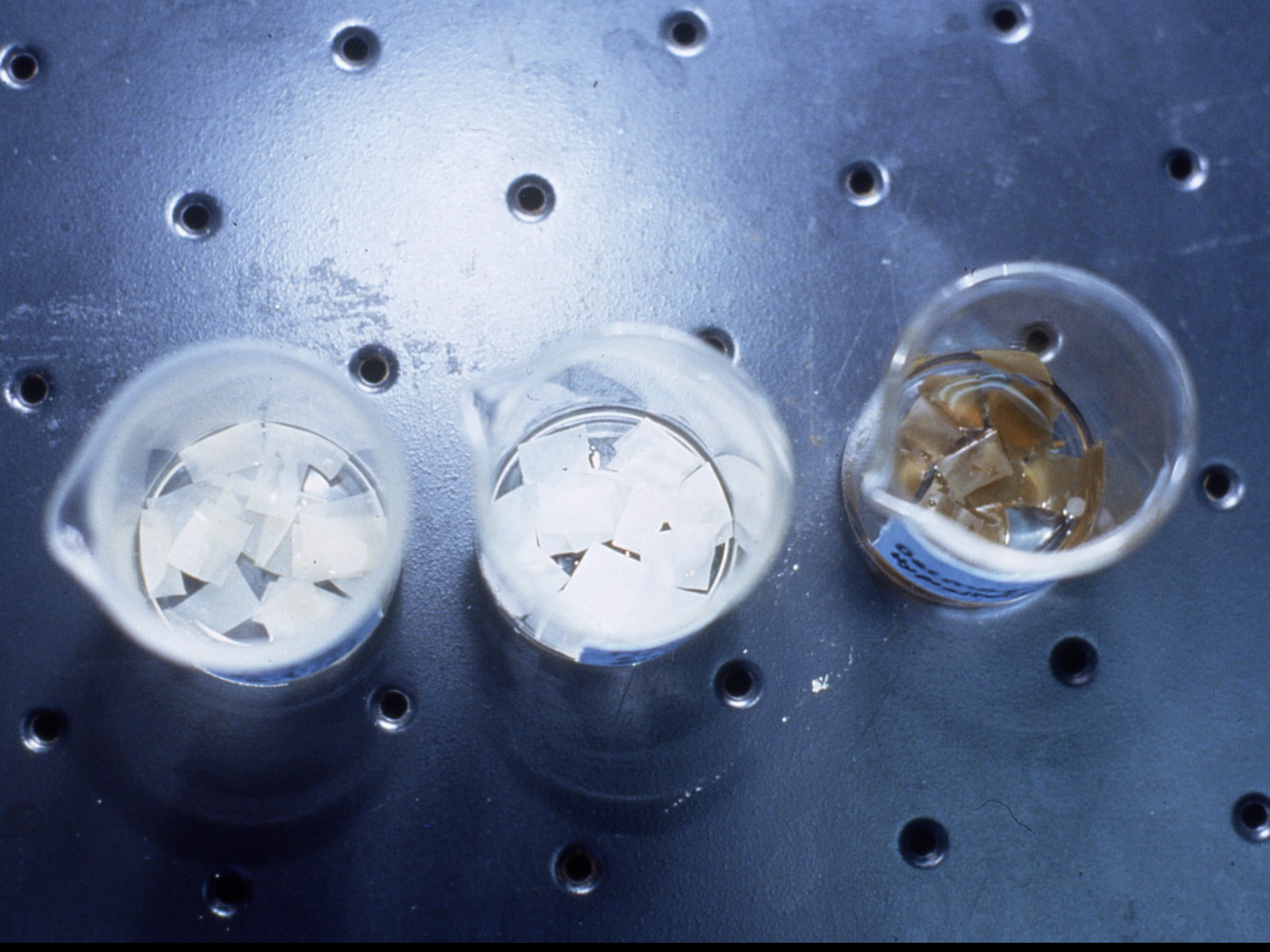

White Latex Surgical Gloves
40ml APPROX.
Plain Exam Gloves
Dermaguard Hypoallergenic



# CORNING

Disposable Sterile
Syringe Filter

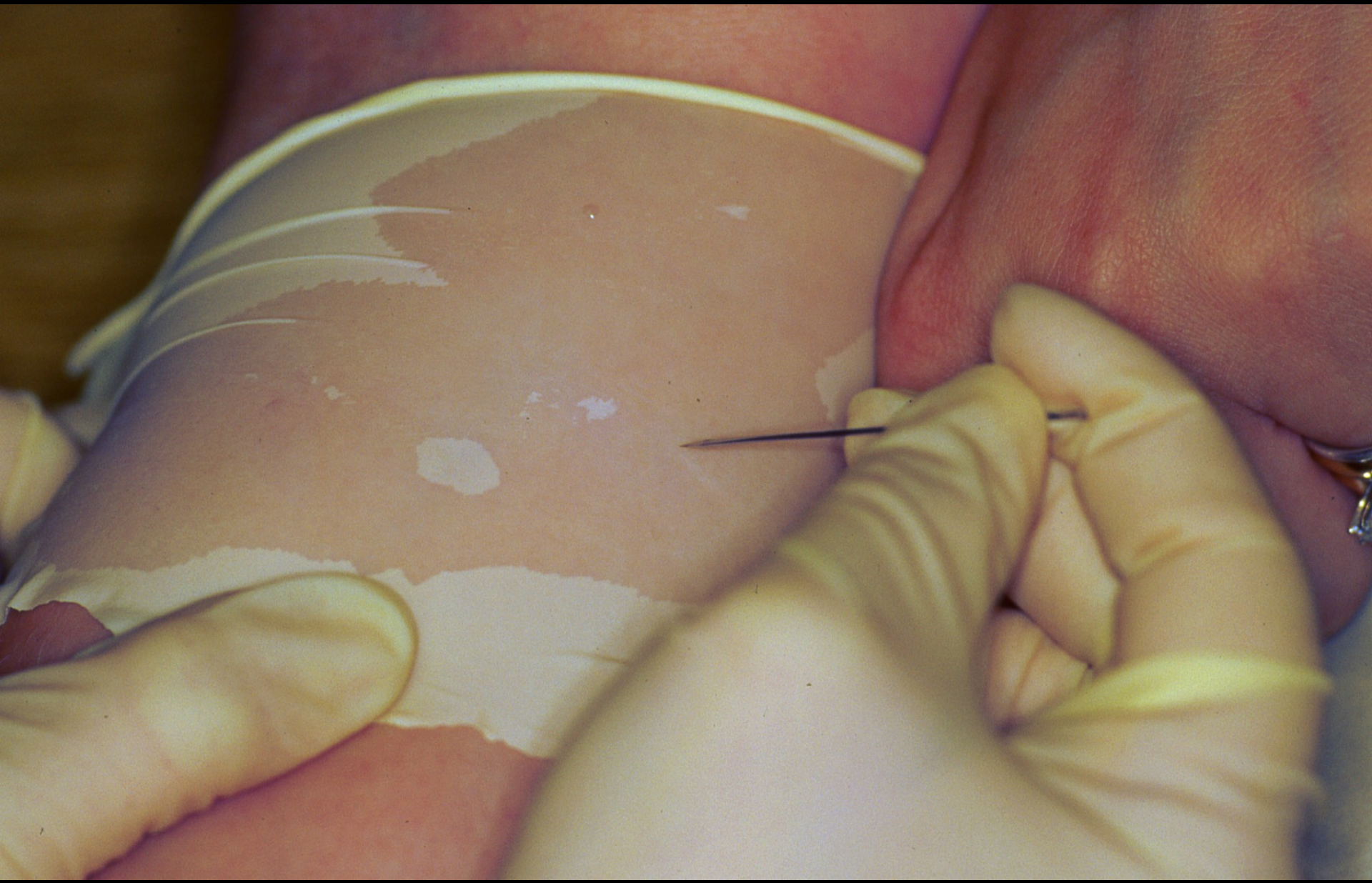
25mm, .20 Micron
Cellulose Acetate Membrane
Acrylic
21052-25
Non-Pyrogenic
75 PSI (5.3 kg/cm²) Maximum Pressure
For Laboratory Use Only

Contents Sterile if Integrity of
Package is Not Compromised

Corning Glass Works, Corning, N.Y. 14831
Made in Japan

Plain
Exam
Glove
B-D
B-D
B-D

# Prick Through The Glove Technique



# Diagnosis--RAST Testing*

- 3 Commercial tests available
  - CAP RAST FEIA (Pharmacia Upjohn)
  - AlaSTAT (Diagnostics Products)
  - HY-TEC-EIA (HYTEC)
- Intra-assay agreement 96%

*JACI 2000;105:1054-62

# Diagnosis--RAST Testing*

- Commercial RAST produced 25-27% false negative results
  - Can diagnose latex sensitivity
  - Inadequate to rule out Latex sensitivity
- Low identification of Hev b 5*
  - Only small amounts of Hev b 5 are present in the diagnostic tests
- Long turnaround time

*JACI 2000;105:1054-62

# Diagnosis--Patch Testing

- Patch testing for type IV reactions

# Diagnosis - “Use” Testing

- "Use test" for contact urticaria

# Therapy

# Therapy

**AVOIDANCE!**

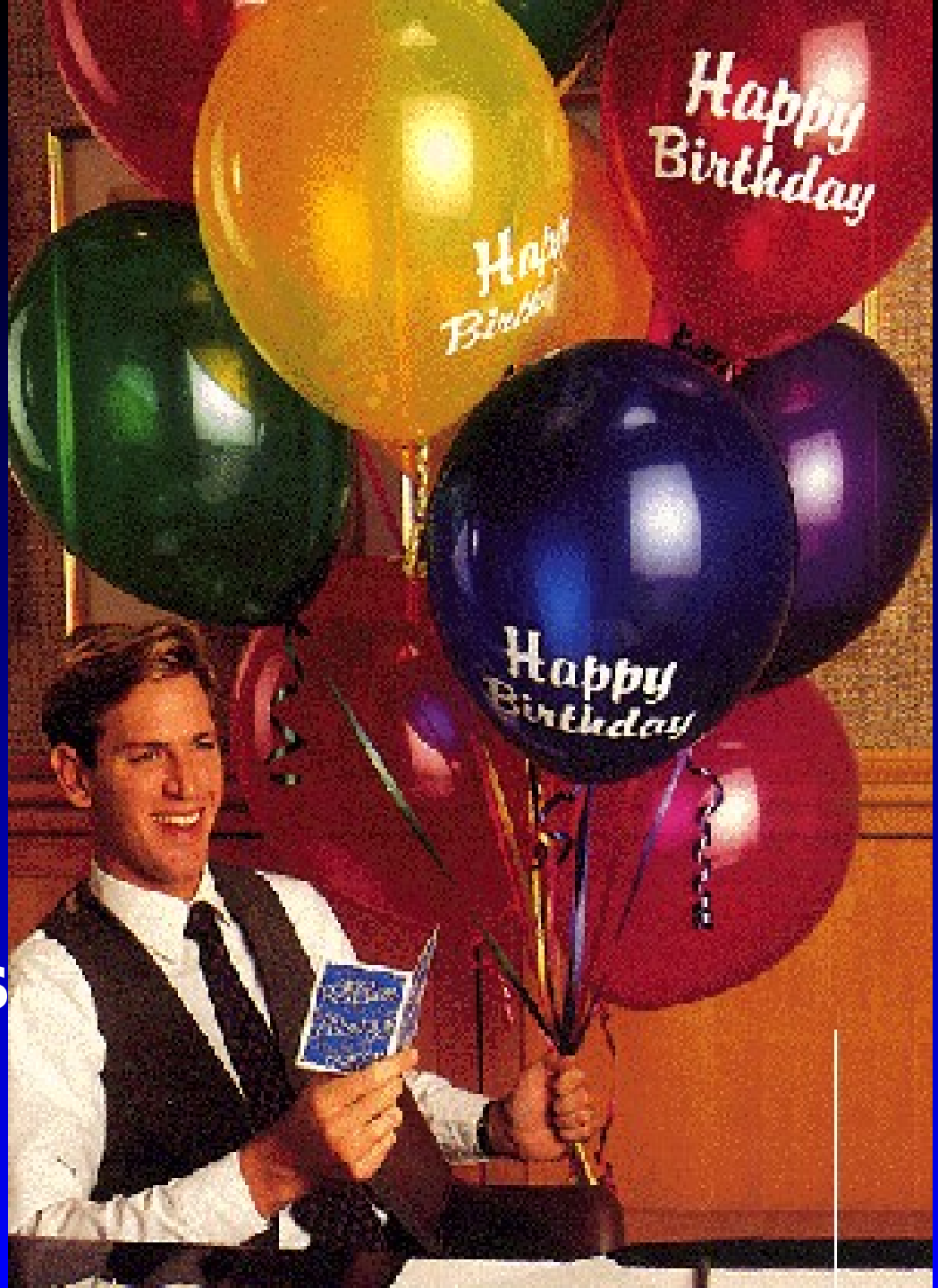
**Avoid Medical Devices that contain latex**

- **Catheters, rubber anesthesia masks etc**
- **?Reactions reported to piston syringes, adhesive tape and multi-dose vials**

# Therapy

## AVOIDANCE!

- Avoid **Non-Medical** devices that contain latex
- Balloons, condoms, gloves, sports equipment, elastics



# Therapy

- Medic Alert bracelet

# Therapy

- EpiPen

# Therapy

- Carry **Non-Latex gloves**

# Alternatives to Latex Gloves

- Many non-latex gloves available
- Hypoallergenic not sufficient, must say “non-latex”
- Tactylon, Elastyren, Vinyl, Nitril

# Nonlatex Glove Properties

- **Vinyl**
  - **Static properties comparable to latex**
  - **Dynamic testing higher failure rate**
- **Stretch Vinyl**
  - **Lower failure rate than vinyl but not equivalent to latex**
- **Nitrile**
  - **comparable to latex in failure testing**
  - **handling characteristics similar to latex**

# Therapy

- **Premedication for surgical procedures**
- ***May not work*, only of theoretical advantage**
  - **Corticosteroids, H1 and H2 blockers**

# Condom Use in Latex Allergic Individuals

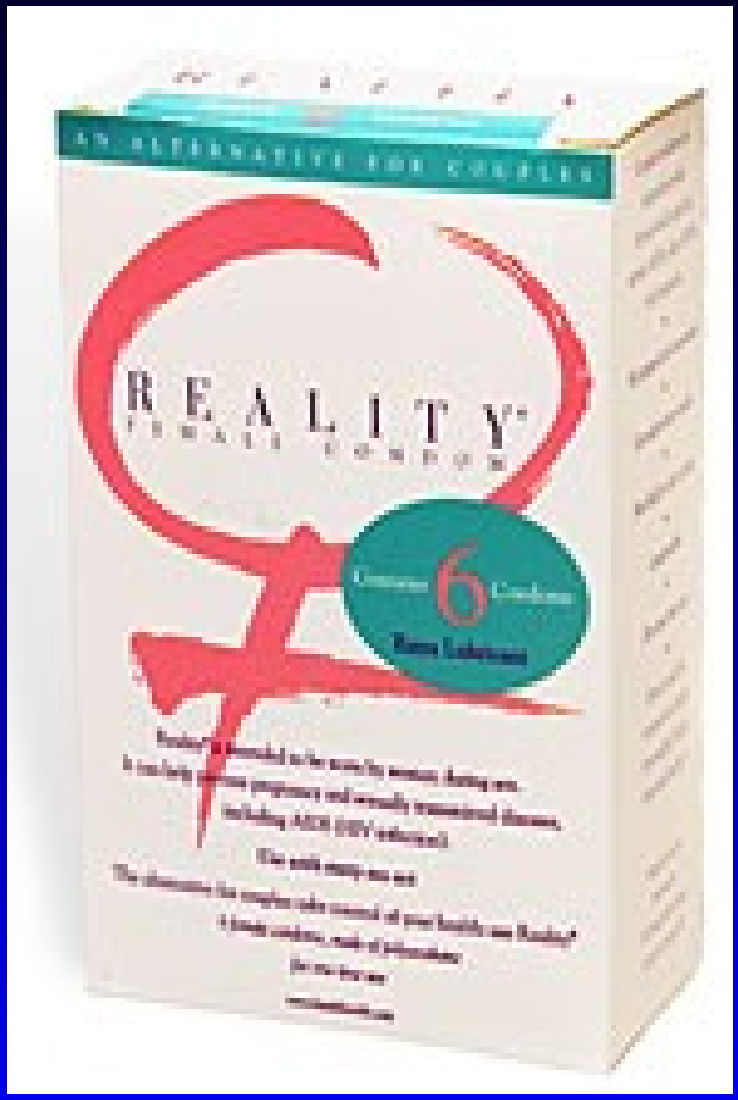
- **Lamb cecum condoms (“skins”) *do not prevent virus transmission***

# Condom Use in Latex Allergic Individuals

- *"Trojan Supra Microsheen"* **Polyurethane** **Condom**

# Condom Use in Latex Allergic Individuals

- Female **polyurethane** condom
  - ***"Reality Female Condoms"***



# Latex Desensitization

- Toci* performed oral rush desensitization on 3 Health Care Workers with latex induced asthma
  - Maintenance 1 mg TID PO
- One discontinued for GI symptoms
- Other 2 have returned to work place successfully with minimal symptoms

*JACI 1998;101:S161

# Latex Desensitization

- Pereira* performed parenteral immunotherapy on a 31 y/o Radiology tech with latex induced allergic rhinitis symptoms
- Parenteral /conventional/rush schedule to maintenance dose of 0.40 μg every 2 weeks
  - Single episode of anaphylaxis during buildup
- Successfully returned to work environment with minimal symptoms

*Allergy 1999;54:291-3

# The Future?

- Identification of Latex allergen epitopes
- **Desensitization** utilizing purified allergens
- **Anti-IgE ?**

# Effect of Omalizumab in Health Care Workers With Occupational Latex Allergy*

- DBPC
- 18 Health care workers with occupational latex allergy
- 9 received omalizumab every 2-4 weeks X 16 weeks, 9 received placebo
- All 9 treated patients were subsequently negative to a conjunctival challenge (0 of placebo)
- Placebo groups subsequently treated with an overall response rate of 94%
- Prick skin testing decreased 49-64%

*JACI 2004;113:360-36

# Recommendations

- Patient history
- Identify risk groups
- Offer diagnostic testing to those in high-risk groups
- AVOIDANCE
- For those with type 1 reaction: Medic Alert bracelet, carry non-latex gloves and autoinjectable epinephrine
- Latex-free areas in health care institutions

# Joint Statement of AAAAI and ACAAI

- **Latex gloves should be used only as mandated by universal precautions standards. Routine use by food handlers, housekeeping, transport and medical personnel should be discouraged**
- **Only low-allergen latex gloves should be purchased and used**
- **Only powder-free latex gloves should be purchased and used**

# Effect Of Reduced Exposure On Natural Rubber Latex Sensitization In Health Care Workers*

- 88 allergic or sensitized Health Care workers
- Avoid latex
- Powder-free NRL gloves for co-workers
- Follow up over 11-34 months

*Annals of All, Ast, Clin Imm 2004;92:530-53

# Effect Of Reduced Exposure On Natural Rubber Latex Sensitization In Health Care Workers*

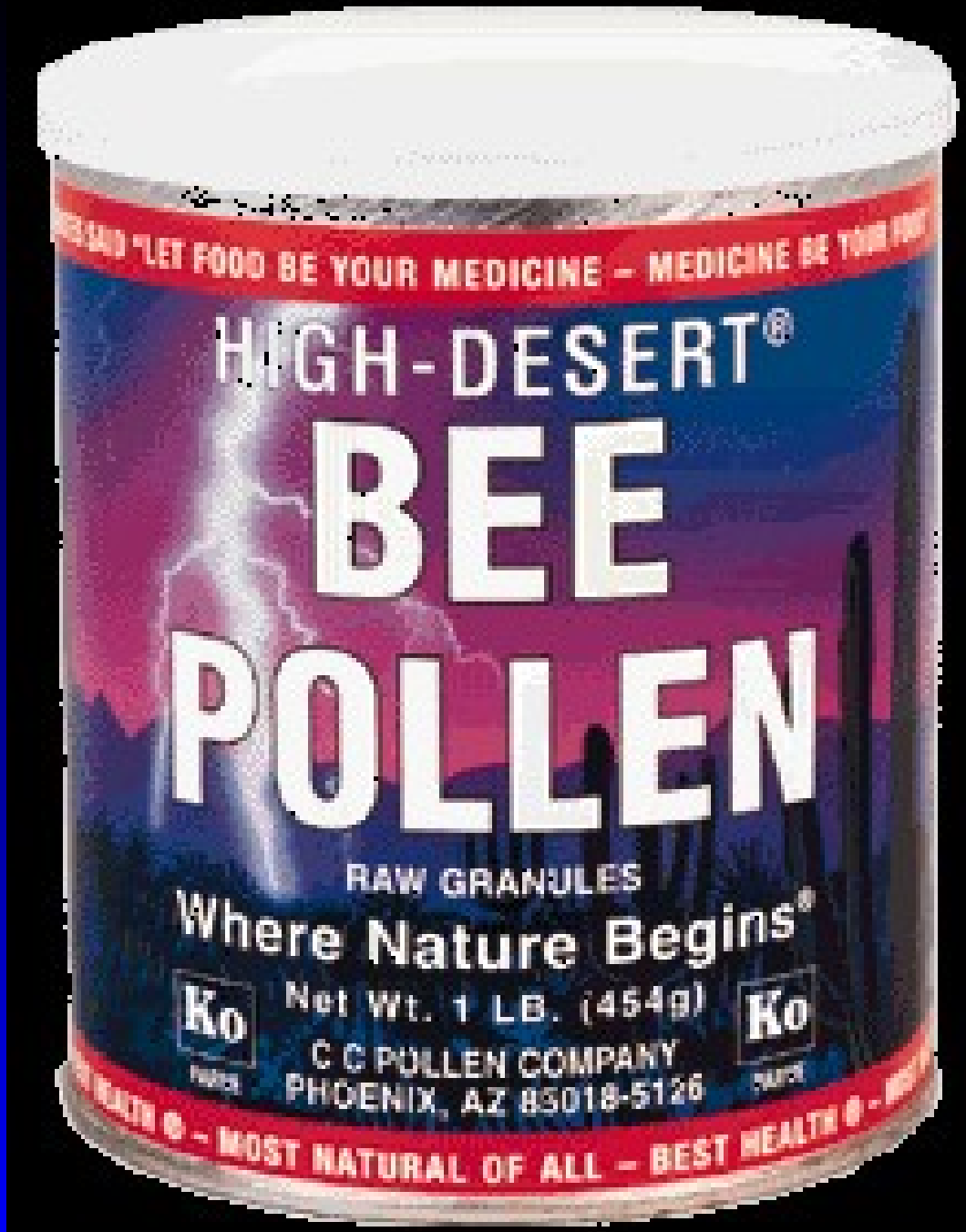
- 1/29 (3.4%) of allergic subjects lost PST reaction
- 16/35 (45.7%) of sensitized subjects lost PST reaction
- 8/25 (32%) allergic subjects developed negative latex RAST
- 14/36 (38.9%) sensitized subjects developed negative latex RAST

*Annals of Allergy, Ast, Clin Imm 2004;92:530

**“Well, this shouldn’t last too**

TEST!

# Does Bee Pollen (orally) work for Allergic Rhinitis?



# Why not?

Can you be allergic to Beer?
SPARE CHANGE FOR BEER!
PLEASE!!

# Beer Allergy

- Made of Malt derived from germinated Barley
- A cause of IgE mediated anaphylaxis
- 2 beer allergens survive the malting and brewing processes

J Allergy Clin Immunol 2001;108:64

- **Does Beer cross react with Broccoli?**

# Beer LTP1 Crossreactivity*

- Peach
- Carrot
- Broccoli
- Apple
- Walnut
- Hazelnut
- Peanut
- Corn
- Rice

*Annals of Allergy 2001;87:65-6

# How do you treat Beer allergy?

# Cautious

# But complications have been reported…

# Can you prevent Beer allergy?

# Prenatal prevention of beer allergy…